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EXAMINER	
STRZELECKA, TERESA E	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 11/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/621,803	BROWNE, KENNETH A.	
	Examiner	Art Unit	
	Teresa E. Strzelecka	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9,19 and 32-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9,19 and 32-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 31, 2005 has been entered.

2. Claims 1-9 and 19 were previously pending. Applicant amended claims 1, 3-7, 9 and 19, cancelled claim 8 and added new claims 32-43. Claims 1-7, 9, 19 and 32-43 are pending and will be examined.

3. Applicant's claim amendments did not overcome any of the previously presented rejections. Applicant's arguments are addressed in the "Response to Arguments" section below.

Response to Arguments

4. Applicant's arguments filed August 31, 2005 have been fully considered but they are not persuasive.

A) Regarding the rejection of claims 1-9 under 35 U.S.C. 102(b) as anticipated by Brennan et al., Applicant argues that the amended claim 1 recites structural features which are not anticipated by Brennan et al. Specifically, Applicant argues that a limitation "wherein no portion of said surface of said solid support is excluded from occupation by an immobilized oligonucleotide, said device having been manufactured by a process comprising immersion of said surface in a liquid composition comprising immobilizable oligonucleotide primers" conflicts with the description of the device of Brennan et al., who teach surface tension arrays comprising patterned hydrophilic and hydrophobic sites, with the hydrophilic sites separated by hydrophobic sites. Applicant further

argues that since the device described by Brennan et al. contains hydrophobic areas which are excluded from occupation by immobilized oligonucleotides, they do not anticipate the claim with this new limitation.

First, let us examine Applicant's own disclosure. On page 8 of the disclosure Applicant discusses the places in the specification which provide support for the new limitation. The pages and line numbers are cited below:

a) page 11, lines 21-23:

"The oligonucleotides or other biomolecules may be attached to surfaces in discrete spots on planar surfaces that characterize microarrays, or over dispersed areas on particulates or planar surfaces."

b) page 14, lines 10-20:

"The immobilized probes and immobilized primers of the composite array also are subject to a preferred distribution pattern. More particularly, the immobilized primers preferably cover the surface of the composite array substantially uniformly except for binding sites on the surface that are occupied by immobilized probe molecules in the array pattern. Unlike the preferred separation of individual spots in the composite array, there is intended to be no spatial separation between the arrayed probes and the immobilized primers. Sites on the solid support surface of the composite array that are not occupied by bonds to the immobilized hybridization probes desirably are occupied by bonds to oligonucleotide primers, thereby resulting in a substantially uniform distribution of primers over the surface of the composite array."

c) page 14, lines 29-30 and page 15, line 1:

"In either case, oligonucleotide primers conveniently may be immobilized to the solid support surface of the probe array by immersion in a liquid composition that includes the oligonucleotides that are to be immobilized."

d) page 15, lines 4-6:

"It is unnecessary to exclude from contact with the primer-containing composition any part of the probe array occupied by immobilized probe molecules."

e) Example 9, page 47, lines 23-30:

"In this procedure the arrayed surface was completely contacted with a solution containing the amplification primer that was to be immobilized. This was done by pipetting the primer-containing solution into the well containing the array, thereby immersing the array so that primers immobilized uniformly over the available plastic surface of well. Plates constructed by this latter method comprised an array of immobilized molecular beacons interspersed among a field of immobilized primers to produce a structure which is referred to herein as a "composite array."

Applicant further adds (page 8 of the response, last two sentences of the first paragraph): "In this instance, the inner bottom surface of a well in a multiwell plate was first derivatized completely (according to the method of Example 5) to facilitate covalent coupling, the coupled with molecular beacon hybridization probes in an array format, and then the completely contacted with a solution containing the amplification primer to be immobilized. Clearly, no portion of the surface of the solid support of the instantly disclosed device was excluded from occupation by an immobilized oligonucleotide."

As can be seen from the above, Applicant does not have support for the new limitation. First, there are a lot of areas which are excluded from occupation by the primers, the most obvious are the areas in which the probes are bound, since the oligonucleotides physically cannot be bound

in the same spots as the probes. Applicant seems to be using the term "support" as meaning a single well of a multiwell plate. For example, on page 15, lines 8-12, Applicant describes the following:

"It should be understood that it is unnecessary to immerse or submerge the entire solid support structure which contains the probe array. Instead, for example, if a probe array is formed on the inner bottom surface of a microtiter well, pipetting into the well an amount of the primer-containing composition sufficient to cover the bottom of the well would be adequate to accomplish immersion of the probe array."

Therefore, the walls separating the wells of the support are excluded from occupation by both the probes and the primers. Even if we take into account the "support" meaning a single well of the multiwell array, there are areas other than the ones occupied by probes which are excluded from oligonucleotide binding. In the cited Example 9 the well of the plate has carboxyl groups to which the modified oligonucleotides can bind. Therefore, the oligonucleotides will only bind in the areas where the groups are present on the surface. Further, if the oligonucleotides are immobilized to derivatized glass slides, as described in Example 2, there are, again, areas which are excluded from occupation by oligonucleotides, since, as can be seen fro Fig. 1, each oligo can only bind to the free sulfhydryl groups.

Now on to the Brennan et al. reference. In this case Applicant chose to understand the term "support" as the whole support of Brennan et al., which is divided into separate areas by, for example, hydrophobic partitions, which, in this case, serve the same purpose as walls between wells in a microtiter plate (page 19, lines 23-25). Further, this is just one embodiment taught by Brennan et al. They teach supports with raised or depressed regions, such as wells (page 15, lines 27-29). Therefore, if one considers the meaning of support as a separate area of the array, which, in Applicant's case is a well of a multiwell plate and in Brennan's case is a single hydrophilic area,

there is no structural difference between these areas of Brennan et al. and Applicant's wells. Brennan et al. describe binding of probes and oligonucleotides to the hydrophilic areas which are derivatized for covalent or non-covalent attachment sites (page 19, lines 6-10 and 16-31; page 25, lines 15-17). The oligonucleotides are attached to the derivatized slides by deposition or synthesis on the array (page 25, lines 18-32; page 26, lines 13-29; page 27, lines 16-29). Finally, in Examples 3 and 4 Brennan et al. describes attachment of oligonucleotides to hydrophilic areas on the array by exposing the whole glass slide to DNA synthesis reagents (page 66, lines 5-32). Therefore, from the structural point of view every derivatized surface able to bind oligonucleotide was exposed to synthesis reagents which resulted in the production of the oligonucleotide, resulting in a product which does not differ structurally from Applicant's.

In conclusion, the limitation of claim 1 "wherein no portion of said surface of said solid support is excluded from occupation by an immobilized oligonucleotide, said device having been manufactured by a process comprising immersion of said surface in a liquid composition comprising immobilizable oligonucleotide primers", as interpreted broadly, does not have the support in Applicant's disclosure, and when interpreted as referring to single, isolated areas of a larger support, does not have a support in the disclosure, either, and is anticipated by Brennan et al.

The rejections are maintained.

B) Regarding the rejection of claim 19 under 35 U.S.C. 103(a) over Brennan et al. and Stratagene catalog, Applicant argues that the rejection is improper since claim 1 is not anticipated or suggested by Brennan et al. The arguments regarding Brennan et al. reference were addressed above.

The rejection is maintained.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-7, 9, 19 and 32-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

A) Claims 1-7, 9, 19 and 32-43 are rejected over the limitation of claim 1"wherein no portion of said surface of said solid support is excluded from occupation by an immobilized oligonucleotide, said device having been manufactured by a process comprising immersion of said surface in a liquid composition comprising immobilizable oligonucleotide primers". As interpreted broadly, i.e., considering the support to encompass the whole device, Applicant did not describe a device which is entirely covered by oligonucleotides. Applicant described a microwell plate in which single wells had oligonucleotides bound to them, not the whole plate, including all the separating walls, side and bottom areas. For example, on page 15, lines 8-12, Applicant describes the following:

"It should be understood that it is unnecessary to immerse or submerge the entire solid support structure which contains the probe array. Instead, for example, if a probe array is formed on the inner bottom surface of a microtiter well, pipetting into the well an amount of the primer-containing composition sufficient to cover the bottom of the well would be adequate to accomplish immersion of the probe array." Similar disclosure is provided in Example 9 on page 47.

Even if we take into account the "support" meaning a single well of the multiwell array, there are areas other than the ones occupied by probes which are excluded from oligonucleotide binding. In the cited Example 9 the well of the plate has carboxyl groups to which the modified oligonucleotides can bind. Therefore, the oligonucleotides will only bind in the areas where the groups are present on the surface. Further, if the oligonucleotides are immobilized to derivatized glass slides, as described in Example 2, there are, again, areas which are excluded from occupation by oligonucleotides, since, as can be seen fro Fig. 1, each oligo can only bind to the free sulfhydryl groups.

Therefore, this limitation introduces new matter into the claims.

B) Claims 32-37 are rejected over the recitation of "said plurality of species of labeled hybridization probes that comprises no more than two species of labeled hybridization probes". This limitation encompasses no more than a single species of hybridization probes, explicitly claimed in claim 33, for which there is no support in the specification. Applicant cites Example 9 as providing support for the limitation of no more than a single probe. However, in this example there are two molecular beacon probes arrayed, one of SEQ ID NO: 7 and one of SEQ ID NO: 5 (page 46, lines 25-30, page 47, lines 1-20).

Therefore, this limitation introduces new matter into the claims.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-7, 9, 19 and 32-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-7, 9, 19 and 32-43 are indefinite in claim 1. Claim 1 is indefinite over the recitation of "wherein no portion of said surface of said solid support is excluded from occupation by an immobilized oligonucleotide, said device having been manufactured by a process comprising immersion of said surface in a liquid composition comprising immobilizable oligonucleotide primers". The term "oligonucleotide" in this expression is considered to mean "amplification primer", since Applicant did not follow the change of terminology introduced in the earlier part of the claim. It is not clear what is meant by this limitation. For example, if the probes are already immobilized on the support before the immobilization of oligonucleotides, the areas with immobilized probes are excluded from occupation by immobilized oligonucleotides. Further, since the claims encompass supports with derivatized sites to which oligonucleotides bind, the areas without derivatized sites will be excluded from occupation by the oligonucleotides.

B) Claims 32-38 are rejected over the recitation of "said plurality of species of labeled hybridization probes that comprises no more than two species of labeled hybridization probes" (claim 32), "said plurality of species of labeled hybridization probes that comprises no more than two species of labeled hybridization probes comprises no more than a single species of labeled hybridization probe" (claim 33), "said plurality of species of amplification primer that comprises no more than a single species of amplification primer" (claims 34, 35 and 38), which are interpreted as none, one or two species for the "no more than two" phrase and none or one species for the "no more than a single species", respectively.

The everyday meaning of the word "plurality" is "a large number" or "a multitude", implying at least two of something. Therefore, it is not clear how a single or no species can be "a plurality of species", since one or zero are definitely not at least two.

Claim Interpretation

9. The term "surface" is interpreted as any area of the support.

10. Applicant did not define the term "species of probes" or "species of primer", therefore they are interpreted as either probes or primers with the same sequence within a species or as probes or primers with different sequences derived from the same target, for example.

11. Applicant did not define the term "immobilized substantially uniformly over a surface", therefore any form of immobilization is considered to result in "substantially uniform" immobilization of nucleic acids over the surface.

12. Applicant did not define the term "within the field of immobilized primers", therefore, any spatial relationship between the immobilized probes and primers is considered to satisfy this limitation.

13. The limitations "no more than two species of labeled hybridization probes" and "no more than a single species of labeled hybridization probe" are interpreted as none, one or two species of probes and none or one species of probes, respectively.

14. The limitation "no more than a single species of amplification primer" is interpreted as none or a single species of the primer.

15. The term "fluid communication" has been described by Applicant on page 9, lines 25-30 of the specification:

"As used herein, two molecules, such as an amplification primer and a hybridization detection probe, are said to be in "fluid communication" with each other when a third species, such as an amplicon, is able to freely interact with either or both of the two molecules. Two molecules that are in fluid communication with each other may, for example, be in the same well of a microplate with no physical barrier between the molecules."

16. The phrase "wherein each of said plurality of species of amplification primer and each of said plurality of species of labeled hybridization probes immobilized to said surface of said solid support is in fluid communication with the others" is interpreted as either the primer species being in fluid communication with each other, or the probe species being in fluid communication with each other or the primer species being in fluid communication with the probe species.

Claim Rejections - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. Claims 1-7, 9 and 32-35 and 37-42 are rejected under 35 U.S.C. 102(b) as being anticipated by Brennan et al. (WO 01/27327; cited in the IDS and in the previous office action), as evidenced by Mueller et al. (Histochem. Cell Biol., vol. 108, pp. 431-437, 1997; cited in the previous office action).

Regarding claim 1, Brennan et al. teach a device for amplifying nucleic acids, the device comprising:

a solid support having a surface (Brennan et al. teach a solid support comprising a surface (page 4, lines 28-32; page 15, lines 16-20).);

a plurality of species of amplification primer immobilized substantially uniformly over said surface, thereby defining a field of immobilized primers, said plurality of species of amplification primer comprising a first amplification primer that comprises a sequence complementary to a first strand of said target nucleic acid (Brennan et al. teach at least one species (= plurality) of

oligonucleotide primer immobilized onto the surface, each of the primer species complementary to each target nucleic acid (page 7, lines 7-14; page 10, lines 23-29).); and

a plurality of species of labeled hybridization probes immobilized to the solid support within said field of immobilized primers (Brennan et al. teach a plurality of probes with sequences the same as or complementary to each target nucleic acid immobilized on the same solid support as the primers (page 7, lines 15-17; page 10, lines 30-33; page 11, lines 1-3). Brennan et al. teach molecular beacon probes which are fluorescently labeled (page 40, lines 32, 33; page 41, lines 1, 2).),

wherein at least one of the said plurality of species of labeled hybridization probes comprises a sequence complementary to an amplicon synthesized using said first amplification primer from said field of immobilized primers and said target nucleic acid as a template in a nucleic acid amplification reaction (Brennan et al. teach capturing of the amplicons synthesized by the immobilized primers using the immobilized capture probes (page 8, lines 27-29; page 9, lines 13, 14; page 10, lines 15, 16). Brennan et al. teach probes and primers immobilized within the same areas (page 38, lines 5-9), therefore they teach probes immobilized within a field of immobilized primers.),

wherein no portion of said surface of said solid support is excluded from occupation by an immobilized oligonucleotide, said device having been manufactured by a process comprising immersion of said surface in a liquid composition comprising immobilizable oligonucleotide primers (This is a product-by-process limitation which might be given weight if the product produced by the process differs from the product taught in prior art. However, in this case there seems to be no difference. Specifically, Brennan et al. teach binding of probes and oligonucleotides to the hydrophilic areas, which are derivatized for covalent, or non-covalent attachment (page 19,

lines 6-10 and 16-31; page 25, lines 15-17). The oligonucleotides are attached to the derivatized slides by deposition or synthesis on the array (page 25, lines 18-32; page 26, lines 13-29; page 27, lines 16-29). Finally, in Examples 3 and 4 (page 65 and 66) Brennan et al. teach attachment of oligonucleotides to hydrophilic areas on the array by exposing the whole glass slide to DNA synthesis reagents (page 66, lines 5-32). Therefore, from the structural point of view every derivatized surface able to bind oligonucleotide was exposed to synthesis reagents which resulted in the production of the oligonucleotide in every available site, resulting in a product which does not differ structurally from Applicant's. Brennan et al. therefore anticipate this limitation.), and

wherein each of said plurality of samples of labeled hybridization probes comprises a detectable label prior to contacting said device with any nucleotide polymerizing enzyme (Brennan et al. teach molecular beacon probes which are fluorescently labeled before an array is contacted with a polymerizing enzyme (page 40, lines 32, 33; page 41, lines 1, 2).).

Regarding claim 2, Brennan et al. teach solid supports made of glass or plastic (page 4, lines 28-30).

Regarding claims 3-5, Brennan et al. teach primers and probes covalently immobilized on the support (page 4, lines 32-34; page 18, lines 2-4).

Regarding claim 6, Brennan et al. teach a reverse primer for the target nucleic acid released from the support, i.e., being soluble (page 6, lines 26-33; page 7, lines 1-3; page 8, lines 1-10).

Regarding claim 7, Brennan et al. teach molecular beacon probes comprising a fluorophor and a quencher (page 40, lines 32, 33; page 41, lines 1, 2).

Regarding claim 9, Brennan et al. do not specifically teach primers comprising a promoter sequence for RNA polymerase, however, they do teach that one of the amplification reactions which can be performed on the primer array is the self-sustained sequence replication (3SR) and

cite Mueller et al. reference (page 37, lines 13-15). As evidenced by Mueller et al., 3SR involves using primers comprising T7 RNA polymerase promoter (Fig. 1), therefore, by teaching 3SR Brennan et al. teach primers comprising RNA polymerase promoters.

Regarding claims 32-35 and 38, Brennan et al. teach at least a single target sequence, which might require different primer sequences to amplify different target regions (page 17, lines 14-19). Since all of these primers are derived from a single target, the can be considered a single species. Therefore, detection probes for such target would also form a single species. Further, Brennan et al. teach primers of similar sequence specific for the same region of target (page 17, lines 19-23). Again, these are considered as single species of primers since they amplify a single sequence. Therefore, Brennan et al. anticipate these limitations.

Regarding claim 37, Brennan et al. teach a flat (= planar) surface (page 4, line 32).

Regarding claim 39, Brennan et al. teach a liquid composition in contact with the device of claim 1 (Fig. 3; page 16, lines 21-34), the composition comprising:

a pH buffer (page 16, line 34),

a DNA polymerizing enzyme (page 16, line 34),

and deoxyribonucleotide triphosphate precursors of DNA (page 16, line 34).

The probes and primers are in fluid communication with each other since there are no physical barriers between them, since the amplified products are captured directly on the probes immobilized to the array (page 38, lines 1-18; Fig. 4, 5).

Regarding claim 40, Brennan et al. teach an RNA polymerase (page 37, lines 12, 13), but do not specifically teach ribonucleotide triphosphates, however, they do teach that one of the amplification reactions which can be performed on the primer array is the self-sustained sequence replication (3SR) and cite Mueller et al. reference (page 37, lines 13-15). As evidenced by Muller

et al., 3SR involves polymerization of an RNA molecule (Fig. 1), and requires ribonucleotide triphosphates (page 435, Table 3), therefore, by teaching 3SR Brennan et al. teach ribonucleotide triphosphates.

Regarding claim 41, Brennan et al. do not specifically T7 RNA polymerase, however, they do teach that one of the amplification reactions which can be performed on the primer array is the self-sustained sequence replication (3SR) and cite Mueller et al. reference (page 37, lines 13-15). As evidenced by Mueller et al., 3SR involves T7 RNA polymerase promoter (Fig. 1), therefore, by teaching 3SR Brennan et al. teach T7 RNA polymerase.

Regarding claim 42, Brennan et al. teach reverse transcriptase (page 37, line 13).

Claim Rejections - 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

20. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Brennan et al. (WO 01/27327; cited in the IDS and in the previous office action), Hu et al. (WO 01/48242; cited in the IDS and in the previous office action) and Stratagene Catalog (p. 39, 1988; cited in the previous office action).

A) Regarding claim 19, Brennan et al. teach the device of claim 1, soluble nucleic acid primers and a control nucleic acid (page 43, lines 31-33), but do not teach kits comprising these elements.

B) Hu et al. teach a kit for nucleic acid amplification on a solid support, the kit comprising a solid support with primers affixed to the solid support and solution phase primers (page 27, 28, [0090]).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have packaged the device of Brennan et al. into a kit form, as suggested by Hu et al. as discussed by Stratagene catalog since the Stratagene catalog teaches a motivation for combining reagents of use in an assay into a kit, "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. Thus one need not purchase gram quantitites of 10 different reagents, each of which is needed in only microgram amounts, when beginning a series of experiments. When one considers all of the unused chemicals that typically accumulate in weighing rooms, desiccators, and freezers, one quickly realizes that it is actually far more expensive for a small number of users to prepare most buffer solutions from the basic reagents. Stratagene provides only the quantitites you will actually need, premixed and tested. In actuality, the kit format saves money and resources for everyone by dramatically reducing waste. 2) The other service provided in a kit is quality control" (page 39, column 1).

21. Claim 36 is rejected under 35 U.S.C. 103(a) as being unpatentable over Brennan et al. (WO 01/27327; cited in the IDS and in the previous office action) and Lund et al. (Nucl. Acids Res., vol. 16, pp. 10861-10880, 1988).

A) Claim 36 is drawn to a method of claim 32 wherein the solid support is a bead. The teachings of Brennan et al. regarding claims 1 and 32 are presented above. Brennan et al. teach solid supports, but do not teach beads.

B) Lund et al. teach DNA probes immobilized on beads (page 10864, last paragraph; page10865; page 10866, paragraphs 1-4).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used beads of Lund et al. as solid supports in the device of Brennan et al. The motivation to do so would have been, as stated by Lund et al.:

"When filters or membranes are used as the support in mixed phase hybridization, the kinetics of hybridization are very slow, ten to twenty fold slower than the corresponding hybridization reaction in solution. By using some sort of particle support which can be kept in a homogenous solution during the hybridization reaction, the kinetics of hybridization will approach those of solution hybridizations." (page 10862, second paragraph), and

"They also provide a large surface area for DNA attachment. In addition, magnetic beads are very easily and rapidly separated from solutions by using a magnet. The beads are kept in the tube with the magnet while solutions are removed or exchanged. This is time saving since centrifugation steps are avoided both during DNA coupling and hybridization reactions." (page 10862, third paragraph).

22. Claim 43 is rejected under 35 U.S.C. 103(a) as being unpatentable over Brennan et al. (WO 01/27327; cited in the IDS and in the previous office action) and Gerard et al. (Mol. Biotech., vol. 8, pp. 61-77, 1997).

A) Claim 43 is drawn to the method of claim 42 where the reverse transcriptase is an MMLV reverse transcriptase. The teachings of Brennan et al. are presented above. They teach reverse transcriptase, but do not specifically teach an MMLV reverse transcriptase.

B) Gerard et al. teach DNA polymerization using an MMLV reverse transcriptase without RNAse H activity (Abstract; page 62, first paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the MMLV reverse transcriptase of Gerard et al. in the liquid composition of

Brennan et al. The motivation to do so, provided by Gerard et al., would have been that MMLV without RNASe H activity synthesized cDNA more efficiently (Abstract).

23. No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E. Strzelecka whose telephone number is (571) 272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

November 3, 2005

TERESA STRZELECKA
PATENT EXAMINER
Teresa Strzelecka